Research Article

Early predictors of developing problematic spasticity following traumatic spinal cord injury: A prospective cohort study

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Objective: To identify early predictors and develop reliable, validated prediction models for development of problematic spasticity after traumatic spinal cord injury (SCI).
Design: Prospective cohort study of the Rick Hansen Spinal Cord Injury Registry (RHSCIR), retrospective review of inpatient medical charts.
Setting: Quaternary trauma center, rehabilitation center, community settings.
Participants: Individuals with traumatic SCI between March 1, 2005, and March 31, 2014, prospectively enrolled in the Vancouver site RHSCIR.
Interventions: None.
Main Outcome Measure: Spasticity limiting function or requiring treatment (problematic spasticity) on the Spinal Cord Injury Health Questionnaire.
Results: In 350 patients, variables documented during hospitalization that predicted the development of problematic spasticity up to 5 years post-injury included: initial Glasgow Coma Scale; age at time of injury; admission to rehabilitation center; community discharge anti-spasticity medication prescription, neurological status, Penn Spasm Frequency Scale, and pain interference with quality of life, sleep, activities; greater change in AIS motor scores between admission and discharge. The predictive models had area under the receiver operating characteristic curve of 0.80 (95% CI 0.75, 0.85) in the development set ($N = 244$) and 0.84 (95% CI 0.74, 0.92) in the validation set ($N = 106$) for spasticity limiting function and 0.81 (95% CI 0.76, 0.85) in the development set and 0.85 (95% CI 0.77, 0.92) in the validation set for spasticity requiring treatment.
Conclusions: Our prediction models provide an early prognosis of risk of developing problematic spasticity after traumatic SCI, which can be used to improve clinical spasticity management and assist research (e.g. risk stratification in interventional trials).

Keywords: Spinal cord injury, Spasticity, Observational study

Introduction

Spasticity, a sensori-motor disorder characterized by intermittent or sustained involuntary muscle activation,[1] is a highly prevalent medical condition that develops in as many as 71% of individuals with traumatic spinal cord injury (SCI).[2,3] The prevalence of "problematic spasticity", defined by spasticity requiring treatment or causing limitation in function, was identified in a large prospective study of individuals with

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traumatic SCI to be as high as 41% up to 5 years post-injury, despite current management strategies.[3] In a large cross-sectional study,[4] spasticity was the fourth most prevalent cause for hospitalization in people with SCI in the previous 12 months.

A goal in treating individuals with SCI is to maximize their function and quality of life by minimizing the effect of secondary complications like spasticity. Being able to predict those who are most likely to develop problematic spasticity can help clinicians appropriately allocate limited resources and researchers focus on testing targeted prevention strategies. To date, there have been no large prospective studies that identify early predictors and create validated predictive models of development of problematic spasticity in individuals with SCI.

The first objective of this study was to identify characteristics of patients, measured during their hospitalization following a traumatic SCI, that are most predictive of problematic spasticity in community follow-up. Variables collected at hospital admission, during the course of hospitalization and on community discharge were analyzed. The second objective was to determine whether results could be used to create a validated predictive model that would accurately predict the development of problematic spasticity in the community.

Methods

Study design

This was a prospective cohort study that utilized patients enrolled at the Vancouver site of the national Rick Hansen SCI Registry (RHSCIR). RHSCIR is a prospective observational database of patients admitted with traumatic SCI to major trauma and rehabilitation centers across Canada.[5] Medication data and selected injury characteristics were confirmed retrospectively using inpatient medical charts from the acute care and rehabilitation hospitals in Vancouver General Hospital, GF Strong Rehabilitation Centre. Ethics approval was obtained from the local Institutional Review Board.

Eligibility criteria

All patients 16 years and over admitted between 2005 and 2014 with traumatic SCI and enrolled into RHSCIR were eligible. Patients were excluded if they died prior to discharge or did not have spasticity data available (see Fig. 1).

RHSCIR and inpatient medical charts review

In this study, socio-demographic factors, injury characteristics, admission and discharge dates, neurological variables, pain and spasticity questionnaire results were abstracted from the RHSCIR datasets. Medication use during hospital admission was collected retrospectively from chart review separately from RHSCIR data abstraction.

Outcome measures

Spasticity at 1, 2, and 5 years post-injury was determined using the Spinal Cord Injury Health Questionnaire (SCI-HQ) (see Appendix A). Our primary outcomes of interest that determined development of "problematic spasticity" were whether patients selected yes or no to: (1) receiving treatment for spasticity or (2) experiencing limitation in activity due to spasticity in the SCI-HQ.

Predictive variables

Many variables are collected for RHSCIR, some of which have been shown in the literature to potentially be predictive of or associated with spasticity (e.g. neurological level and AIS grade, motor score;[6,7] pain;[8] age, sex and medication use[7]). Variables included in the analysis were selected *a priori* (Table 1). We chose to include Gabapentin use in the month following SCI as a possible predictor of spasticity development due to the recent reports in the literature demonstrating that early use of anticonvulsants, in particular, gabapentinoids such as Gabapentin, may improve motor recovery post SCI.[9,10] Variables that were analyzed in addition to demographics and neurological status at admission and community discharge included the first Glasgow Coma Scale (GCS) taken at the scene of the accident (GCS Field) and at the admitting hospital (GCS Facility); GCS between 13 and 15 was categorized as mild, 9–12 was moderate and 3–8, severe. The presence of spasticity within two weeks of community discharge was determined using Part 1 of the Penn Spasm Frequency Scale (PSFS), a self-report measure of spasticity-related muscle spasms (see Appendix A).[11,12] Patient-rated pain interference with sleep, normal activities and quality of life was captured using a 0–10 Numeric Rating Scale (NRS, 0 = no interference, 10 = the most interference imaginable; levels categorized as mild if NRS 1–3, moderate if NRS 4–6, and severe if NRS 7–10) at community discharge.[13] Patients were considered to be on anti-spasticity medication at community discharge if they had one or more of: (1) an oral medication prescribed for the purpose of spasticity management (e.g. Baclofen, Tizanidine, Diazepam, Clonazepam, or Dantrolene); (2) a botulinum toxin injection for spasticity within the last 90 days[14,15] or (3) a phenol injection for spasticity within the last 6 months.[16] The neurological data were collected by trained clinicians. The change in AIS motor score was calculated by subtracting the

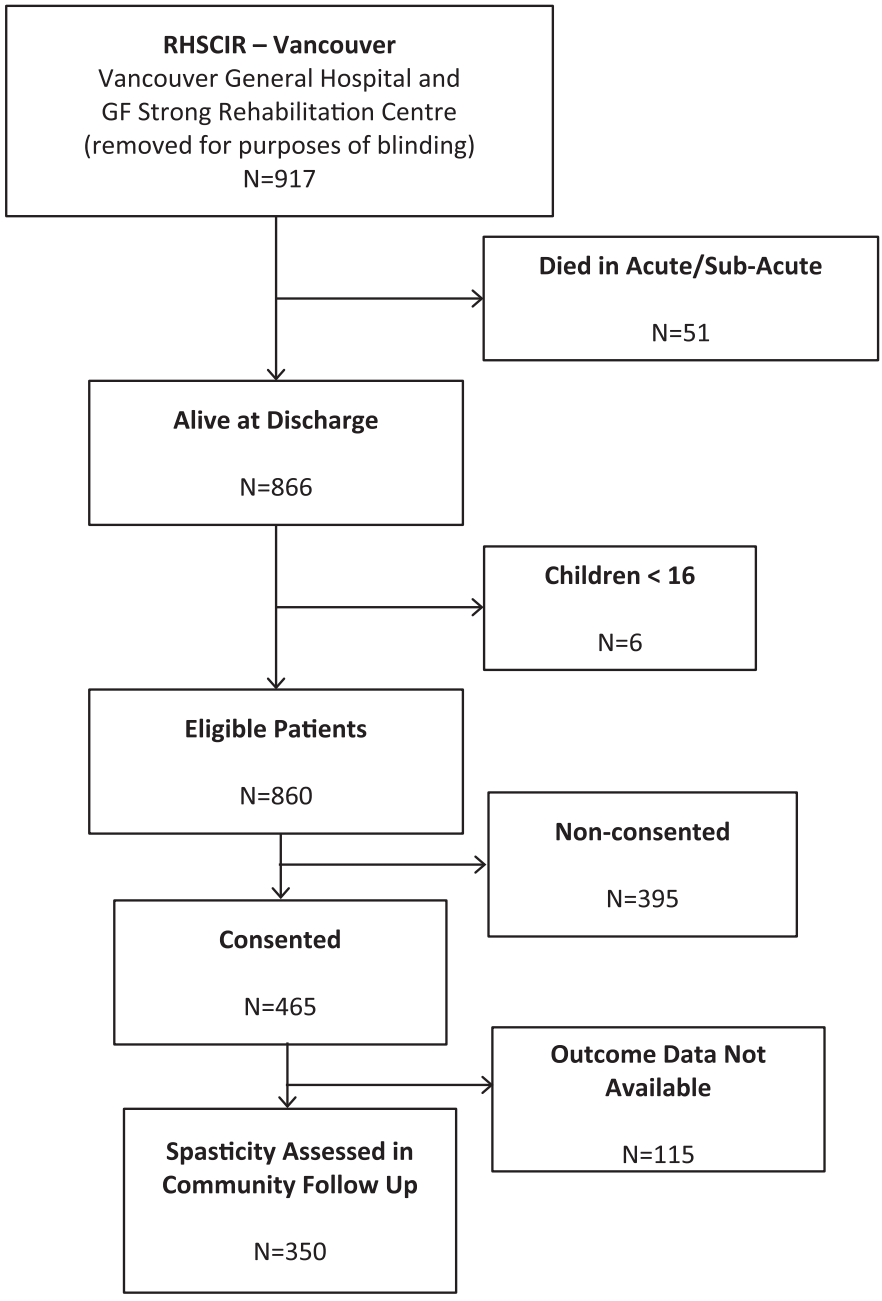


Figure 1 Study flowchart.

initial (within 72 hours of admission) motor score from the final (community discharge) motor score.

Statistical analysis

The objective of the analysis was to identify the patient characteristics that are most predictive of spasticity in community follow-up. To identify important predictors, we fit elastic net logistic regression models,[17] which "select" characteristics associated with the outcome, problematic spasticity in community follow-up. We utilized Variable Importance Probabilities to measure the importance of characteristics, where the importance of a characteristic is measured by the number of times it is "selected" in the models fit in 1,000 bootstrap samples.[18] Characteristics that are important will be selected most often by the models when re-sampling the data. When fitting the models, the elastic net tuning parameter was chosen by tenfold cross-validation using area under the receiver operating characteristic (ROC) curve as the prediction criterion.

To account for the drop-off in response during community follow-up, inverse-probability weights of response during community follow-up were estimated. Patients that were less likely to have community follow-up data

Table 1 Patient characteristics for potential spasticity predictors.

Category	Characteristic	Level	Overall (*N* = 350)
Admission			
Demographics	Sex (%)	Female	82 (23.4)
		Male	268 (76.6)
	Age (years) (median [IQR])		43.0 [27.0, 57.0]
	Age (years) (%)	16–30	113 (32.3)
		31–45	83 (23.7)
		46–60	92 (26.3)
		61–75	52 (14.9)
		76+	10 (2.9)
	Household Income (%)	≥ 20K	210 (60.0)
		< 20K	39 (11.1)
		Unknown	101 (28.9)
	Education (%)	No Diploma or G.E.D	77 (22.0)
		Diploma	272 (77.7)
		Unknown	1 (0.3)
	Living arrangement (%)	Alone	84 (24.0)
		Not alone	263 (75.1)
		Unknown	3 (0.9)
Trauma	GCS facility (%)	Mild	277 (79.1)
		Moderate	6 (1.7)
		Severe	35 (10.0)
		Unknown	32 (9.1)
	GCS field (%)	Mild	263 (75.1)
		Moderate	14 (4.0)
		Severe	31 (8.9)
		Unknown	42 (12.0)
Medical History	Cannabis use at Admission (%)	No	304 (86.9)
		Yes	46 (13.1)
	Comorbidities (%)	None	261 (74.6)
		At least one	88 (25.1)
		Missing	1 (0.3)
Discharge			
Neurology	Motor neuro level (%)	C1–C8	200 (57.1)
		T1–T12	94 (26.9)
		L1–S5	39 (11.1)
		C1–T12 + L1–S5	1 (0.3)
		Unknown	16 (4.6)
	AIS (%)	A	109 (31.1)
		B	48 (13.7)
		C	38 (10.9)
		D	147 (42.0)
		E	3 (0.9)
		Unknown	5 (1.4)
	AIS motor score (points) (%)	Unknown	13 (3.7)
		Known	337 (96.3)
	AIS motor score (points) (median [IQR])		52.0 [39.0, 83.0]
	AIS UEMS (points) (%)	Unknown	7 (2.0)
		Known	343 (98.0)
	AIS UEMS (points) (median [IQR])		44.0 [28.0, 50.0]
	AIS LEMS (points) (%)	Unknown	8 (2.3)
		Known	342 (97.7)
	AIS LEMS (points) (median [IQR])		12.0 [0.0, 41.0]
	Change in AIS motor score (points) (%)	Unknown	36 (10.3)
		Known	314 (89.7)
	Change in AIS motor score (points) (median [IQR])		7.0 [0.0, 23.0]
	Neurological level (%)	C1–C8	206 (58.9)
		T1–T12	94 (26.9)
		L1–S5	42 (12.0)
		C1–T12 + L1–S5	2 (0.6)
		Unknown	6 (1.7)

Continued

Table 1 ***Continued.***

Category	Characteristic	Level	Overall (*N* = 350)
Course of care	Length, inpatient stay (days) (median [IQR])		132.0 [76.2, 212.0]
	Gabapentin, within 1 month (%)	No	110 (31.4)
		Yes	196 (56.0)
		Unknown	44 (12.6)
	Operation (%)	No	55 (15.7)
		Yes	295 (84.3)
	Rehab (%)	No	47 (13.4)
		Yes	303 (86.6)
	Length, rehab (days) (median [IQR])		85.5 [48.0, 147.0]
Pain	Pain, activity (%)	None	85 (24.3)
		Mild	94 (26.9)
		Moderate	95 (27.1)
		Severe	53 (15.1)
		Unknown	23 (6.6)
	Pain, QOL (%)	None	86 (24.6)
		Mild	97 (27.7)
		Moderate	83 (23.7)
		Severe	60 (17.1)
		Unknown	24 (6.9)
	Pain, sleep (%)	None	111 (31.7)
		Mild	99 (28.3)
		Moderate	69 (19.7)
		Severe	50 (14.3)
		Unknown	21 (6.0)
Spasticity	PSFS (%)	0	98 (28.0)
		1	108 (30.9)
		2	56 (16.0)
		3	57 (16.3)
		4	18 (5.1)
		Unknown	13 (3.7)
	Discharge anti-spasticity medication (%)	No	231 (66.0)
		Yes	119 (34.0)

UEMS, upper extremity motor score; LEMS, lower extremity motor score.

were upweighted compared to patients that were more likely to have responded during community follow-up.

To identify the most important characteristics, the data were split into two sets: a development set, consisting of 70% of the full dataset, and a validation set, consisting of the remaining 30% of the observations. The development sets were analyzed to identify clinical characteristics that predict each outcome (objective 1). Then, using the most important variables identified in the development data, final predictive models and nomograms were created and the predictive performance of the final models was assessed in the validation set (objective 2). The proportion of development versus validation set was determined *a priori*. To estimate the direction of the effect of each clinical characteristic on the outcomes, odds ratios and associated confidence intervals (CIs) for each characteristic and outcome were calculated in the development sets. Most important variables were determined *a priori* to be those with Variable Importance Probabilities greater than or equal to 75%.

The inverse-probability weighted logistic elastic net models were fit using the glmnet package in R.[19] Odds ratios and associated inverse-probability weighted confidence intervals (CIs) were calculated using the survey package in R.[20] Nomograms from the final predictive models were constructed using the rms package[21] and weighted areas under the curve and associated bootstrap CIs were calculated using the Weighted ROC package in R.[22]

Results

The cohort used in the final data analysis was $N = 350$ (see Fig. 1). Patient characteristics at admission and discharge are reported in Table 1. Mean age was 46 ± 19 years. Mean time from injury to community discharge was 108 ± 95 days (range 1–728 days). Stratification of neurological levels of injury was based on previous work by this group.[3] The most common mechanisms of injury were falls ($N = 120$), transport ($N = 114$), sports ($N = 80$), and assault ($N = 14$). Of the 350 patients included in the cohort, 335 had GCS reported. Of the 335, 101 (30.1%) had a documented GCS Field < 15. Of the total cohort, 142 (40.6%) patients were treated with Botox, Phenol or an oral anti-spasticity medication during their inpatient

stay. An increase in AIS motor score from admission to community discharge occurred in 226 patients. In these patients, 127 (56.2%) had problematic spasticity in community follow-up, while 60 (68.2%) of the 88 patients whose AIS motor score did not improve had problematic spasticity in community follow-up. There were 36 patients on whom change in motor score was unknown. Patients with AIS A injuries at discharge were less likely to have had a motor score improvement compared to AIS B, C or D injuries (Holm adjusted P values for multiple comparisons $P = 0.048$ for A compared to B, $P < 0.001$ for A compared to C and D from Fisher's exact test). Patients with T1–T12 neurological levels at discharge were less likely to have experienced motor score improvement compared to patients with C1–C8 or L1–S5 neurological levels at discharge (adjusted $P < 0.001$ for both comparisons). The same was true for T1–T12 motor score at discharge compared to C1–C8 or L1–S5 (adjusted $P < 0.001$ for both comparisons).

The estimated odds ratios and Variable Importance Probabilities in the development data sets are displayed in Figs 2 and 3 with detailed data provided in Appendix B.

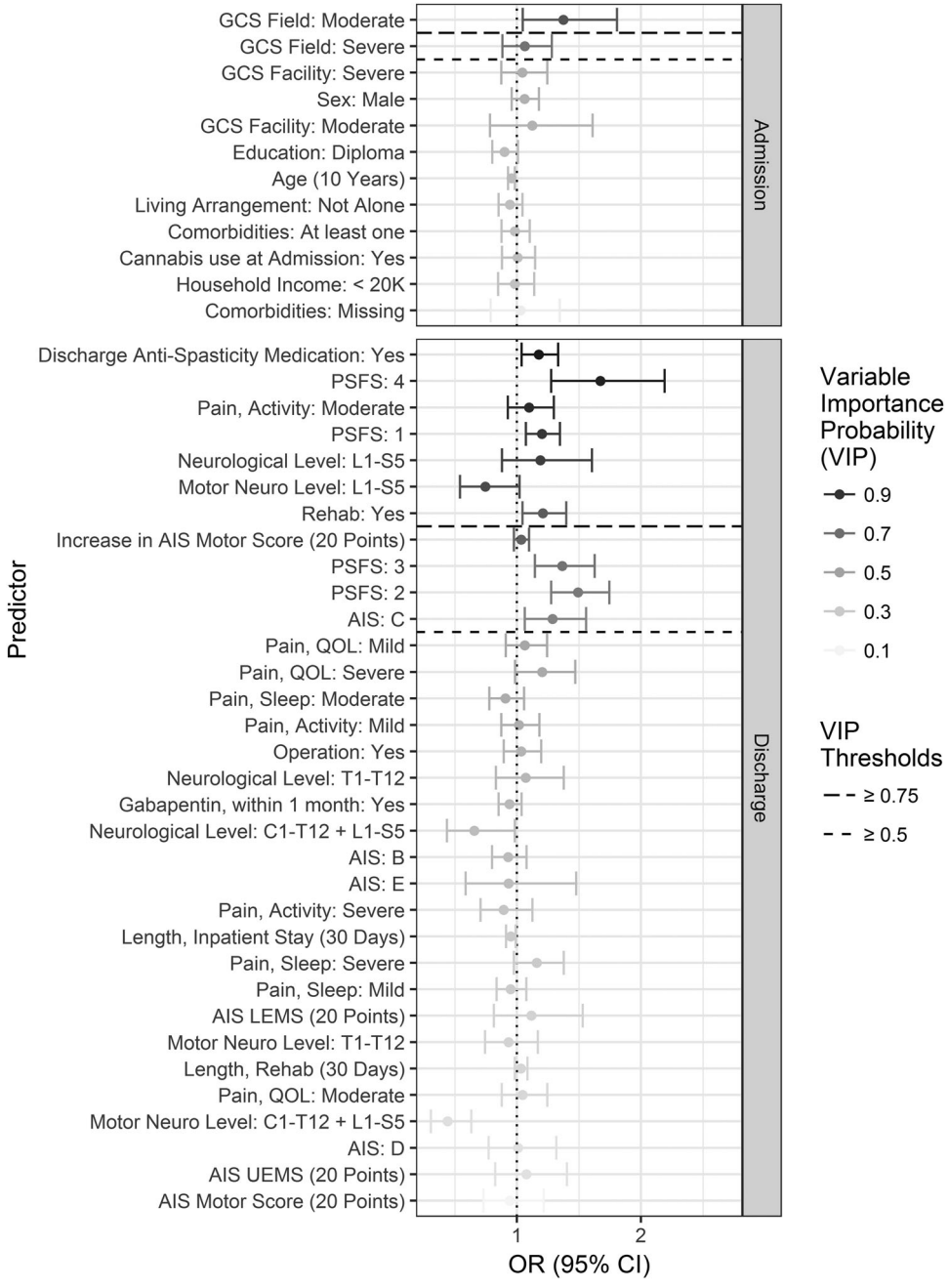


Figure 2 Estimated odds ratios and variable importance probabilities (VIP) in the development data set for spasticity requiring treatment on community follow-up.

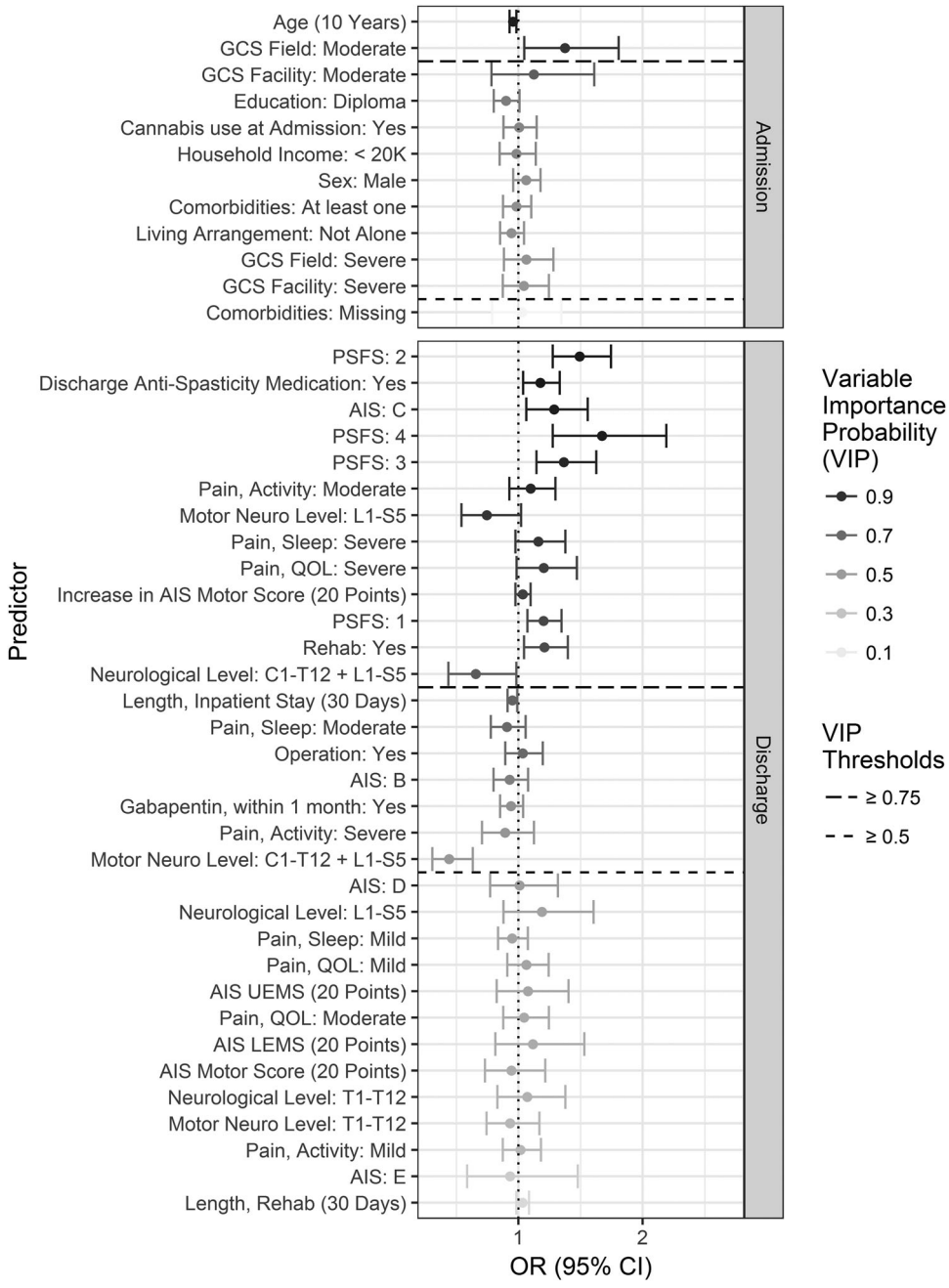


Figure 3 Estimated odds ratios and variable importance probabilities (VIP) in the development data set for spasticity limiting function on community follow-up.

Predictors for developing spasticity requiring treatment

$N = 7$ variables were identified as the most predictive (Variable Importance Probabilities greater than or equal to 75%) for either increasing or decreasing the risk of developing spasticity requiring treatment on community follow-up up to 5 years post-injury. Predictors on hospital admission and during the course of hospitalization that increased the risk were identified as: (1) moderate GCS Field (OR 1.38, 95% CI 1.05, 1.81) and (2) admission to the rehabilitation center from acute care (OR 1.21, 95% CI 1.05, 1.40). Predictors at community discharge that increased the risk included: (3) prescription of spasticity medication (s) (OR 1.18, 95% CI 1.04, 1.33); (4) moderate pain during activities (OR 1.10, CI 95% 0.93, 1.30); (5) PSFS 1 (OR 1.20, 95% CI 1.07, 1.35) or 4 (OR 1.67, CI 95% 1.28, 2.19). Predictors at community discharge that decreased the risk were (6) neurological level of L1–S5 and (7) motor level of L1–S5. Variables that

almost reached the cut off for statistical significance for increasing risk of spasticity included GCS Field severe (Variable Importance Probability 68%), increase in AIS motor score equal to or greater than 20 (Variable Importance Probability 74%) and PSFS 2 or 3 (Variable Importance Probability 66% and 68%, respectively). See Appendix B for detailed data on odds ratios and CIs for each variable analyzed.

Predictors for spasticity limiting function

$N = 12$ variables were identified as the most predictive for either increasing or decreasing the risk of developing spasticity limiting function on community follow-up. A variable known at hospital admission that increased the risk was (1) GCS Field moderate. A variable at hospital admission that decreased the risk was (2) older age; for each 10-year increase in patient age at time of injury, the probability of developing spasticity limiting function at community follow-up decreased by 4% (OR 0.96, 95% CI 0.93, 0.98). A predictor during the course of hospitalization that increases the risk was (3) admission to the rehabilitation center (OR 1.21, 95% CI 1.05, 1.40). Characteristics known at community discharge that predicted an increased risk were (4) PSFS 1, 2, 3 or 4; (5) prescription of spasticity medication(s) at discharge; (6) increase in AIS motor score equal to or greater than 20; (7) AIS grade C; (8) severe pain affecting quality of life; (9) severe pain affecting sleep; and (10) moderate pain during activities. Characteristics known at community discharge that predicted a decreased risk were (11) neurological level C1–T12 + L1–S5 (where one patient has two levels of injury, one resulting in neurological level within C1–T12 and the other resulting in a neurological level within L1–S5), and (12) motor level L1–L5.

Predictive models for problematic spasticity in community follow-up

Nomograms from the final predictive models are presented in Figs 4 and 5. The final predictive models had an area under the ROC curve for predictors of spasticity requiring treatment of 0.80 (95% CI 0.76, 0.85) in the development set ($N = 244$) and 0.85 (95% CI 0.77, 0.92) in the validation set ($N = 106$), and for predictors of spasticity limiting function of 0.81 (95% CI 0.75, 0.85) in the development set and 0.84 (95% CI 0.74, 0.92) in the validation set. An example of how to use the nomogram for estimating the risk of spasticity limiting function is provided in Fig. 6.

Discussion

This is the first large prospective cohort study to identify early predictors of the long term (up to 5 years post-injury) development of problematic spasticity in individuals with traumatic SCI. This is also the first study to create models that predict the development of problematic spasticity in the community with excellent discrimination on validation analysis. In summary, variables documented during hospitalization included: at time of injury age and first documented Glasgow Coma Scale; whether admitted to rehabilitation center prior to community discharge or discharged direct from acute care hospital to community (e.g. home, long-term care facility); whether at time of discharge

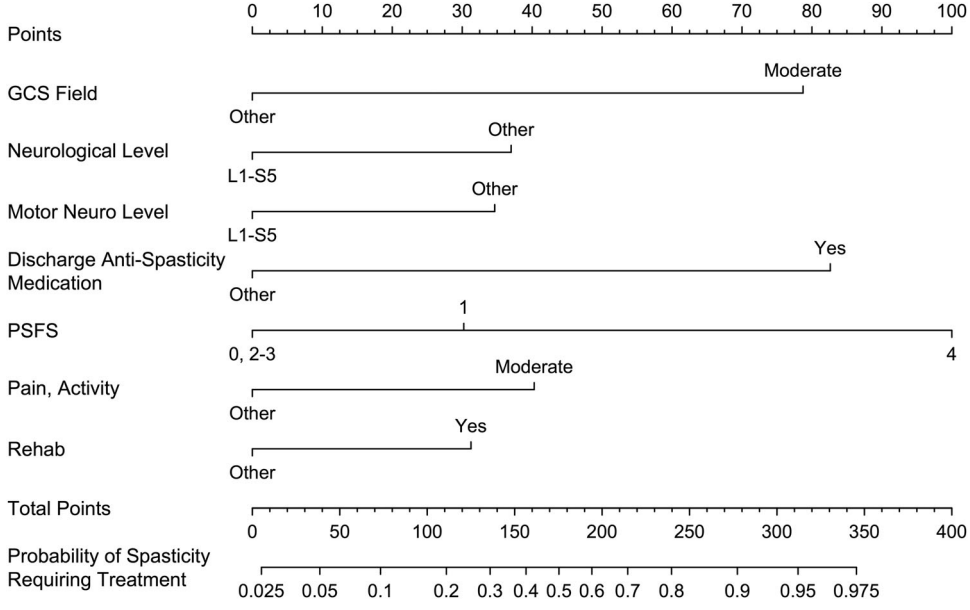


Figure 4 Nomogram for the predictive model of spasticity requiring treatment on community follow-up.

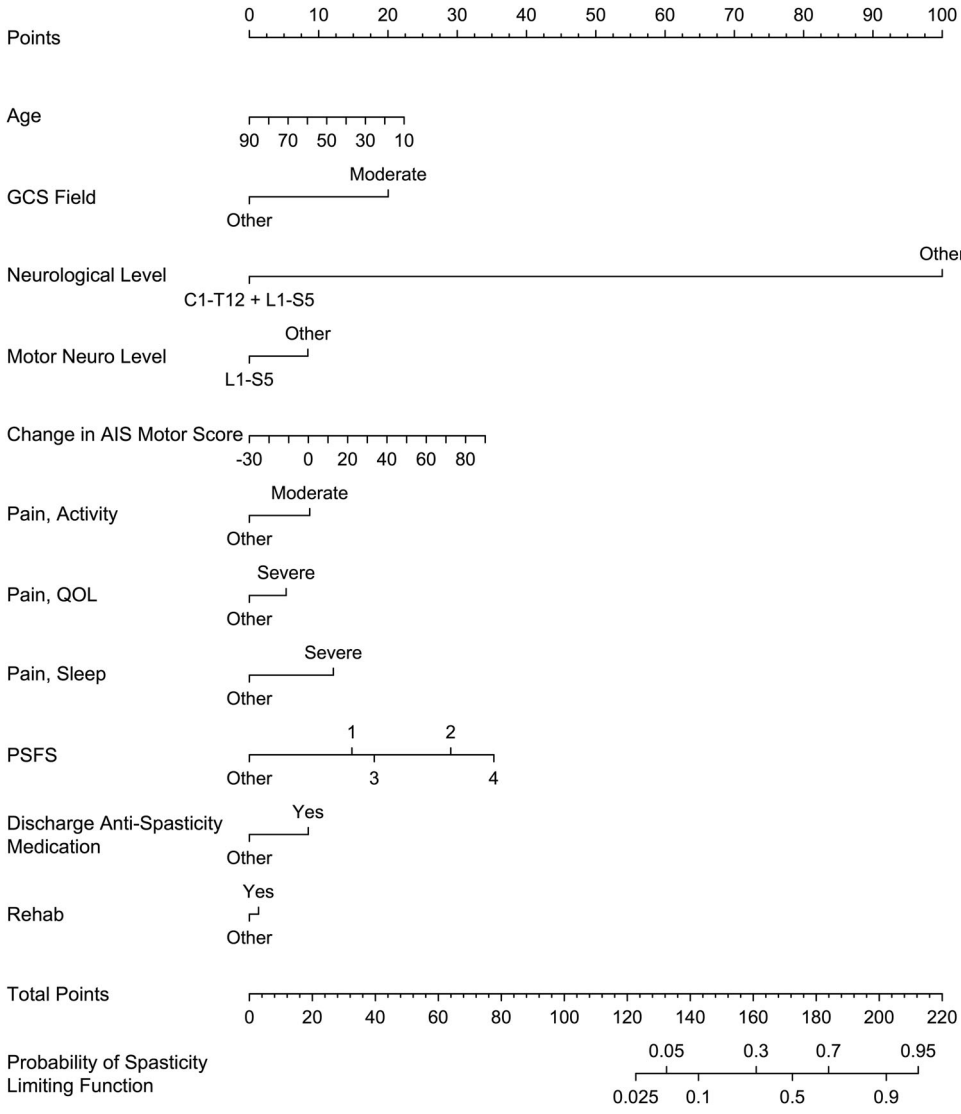
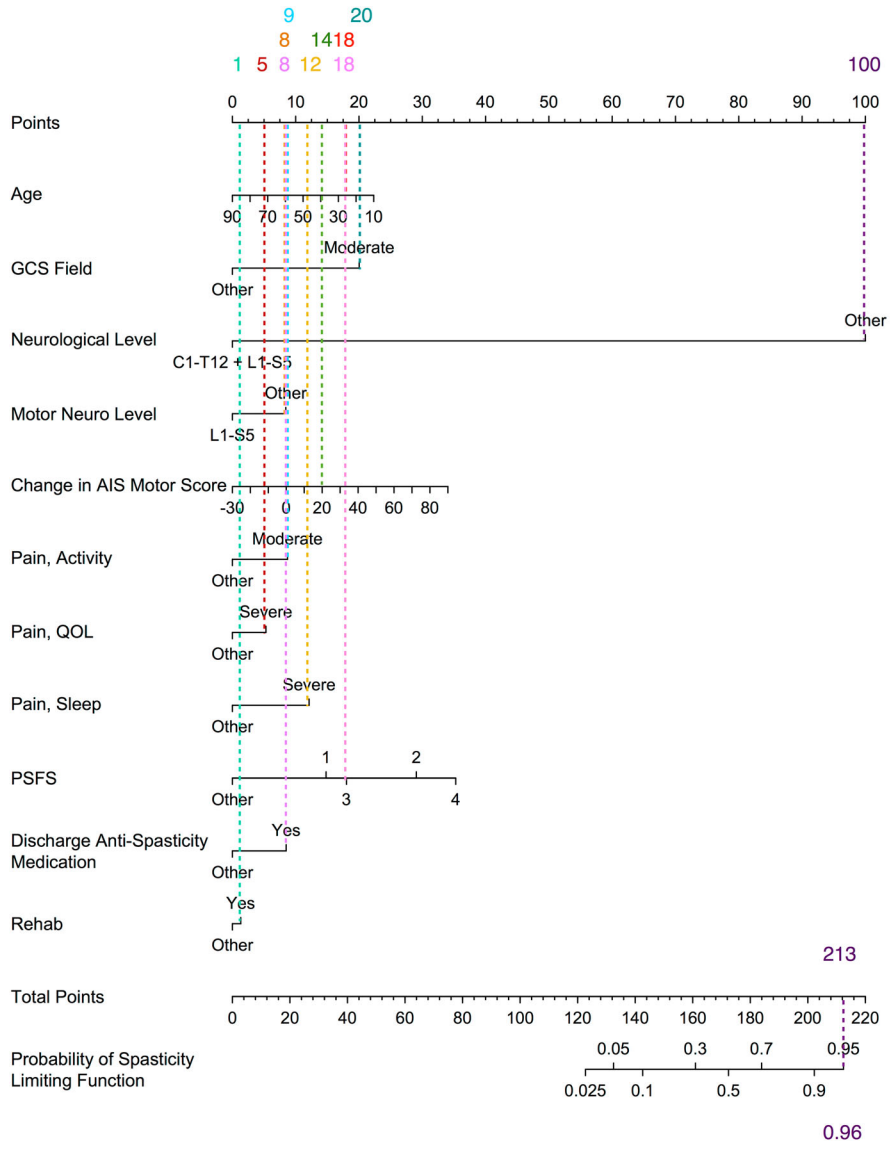


Figure 5 Nomogram for the predictive model of spasticity limiting function on community follow-up.

to community the person was on anti-spasticity medication; at time of community discharge neurological status (*i.e.* neurological level, motor level, AIS grade and change in AIS motor score), score on the Penn Spasm Frequency Scale, and self-reported pain interference with activities, sleep and quality of life.

Neurological predictors like more severe GCS and sparing of lower motor nerves are consistent with what is expected pathophysiologically based on spasticity occurring as a result of injury to the central nervous system. The odds ratios in the tables are conditional on all other variables, therefore results suggest that for a given AIS or neurological level at discharge, a greater improvement in motor score was associated with increased odds of problematic spasticity in community follow-up. Among patients with motor score improvement, patients with AIS C, problematic spasticity at discharge and those who had rehab were most likely to have problematic spasticity in community follow-up. The finding of a greater change in AIS motor score being predictive of increased risk of developing problematic spasticity is consistent with the findings by a study by Dvorak *et al.*[6] who studied individuals with traumatic central cord syndrome. Not only was a greater change in AIS motor score associated with increased risk of spasticity requiring medication for treatment (in other words, problematic spasticity) it was also associated with decreased quality of life (as measured by the SF-36) and functioning (as measured by the Functional Independence Measure). This was a very interesting finding, as one might expect that greater AIS motor recovery would be associated with improved quality of life and functioning. However, it appears that problematic spasticity can prevent the individual from



Variable	Value	Points
Age	25	18
GCS Field	Moderate	20
Neurological Level	Other	100
Motor Neuro Level	Other	8
Change in AIS Motor Score	20	14
Pain, Activity	Moderate	9
Pain, QOL	Severe	5
Pain, Sleep	Severe	12
PSFS	3	18
Discharge Anti-Spasticity Medication	Yes	8
Rehab	Yes	1
Total Points		**213**
Probability of Spasticity Limiting Function		**0.96**

Figure 6 Example use of nomogram for spasticity limiting function on community follow-up. An example case is provided for a hypothetical individual who acquires a traumatic SCI with values provided for the most important variables (e.g. 25 years old at time of injury, first GCS of at scene of accident = 10, etc).

optimizing use of available motor strength, presumably due to the spasticity-related intermittent or sustained involuntary muscle contractions. These results are further supported by a study by our group demonstrating that individuals with AIS C (incomplete motor and sensory SCI) had the highest prevalence of problematic spasticity on community discharge.[3] A comprehensive review on the pathophysiological changes following SCI that contribute to development of spasticity[23] describes that while motor neuron adaptation to loss of supraspinal input can occur following SCI, changes can be maladaptive resulting in uncontrolled muscle activation (e.g. spasticity) thus impairing function, which generally requires controlled or purposeful muscle activation. Therefore, it stands to reason that motor recovery can be associated with an increase in both adaptive (controlled) and maladaptive (uncontrolled) muscle activation, and that it is important to identify those who are at greatest risk for experiencing maladaptive motor recovery so as to target preventative treatment strategies that will optimize function and, ultimately, quality of life.

Increased age at time of injury being "protective" of developing spasticity was an interesting finding. A large longitudinal study ($N = 1790$) of individuals with chronic traumatic SCI also identified age as negatively associated with self-reported spasticity severity.[24] Further research is needed to ascertain why this may be the case.

Admission to the rehabilitation center as compared to being discharged to the community directly from the acute care hospital was associated with an increased risk of developing problematic spasticity in the community. This is probably as a result of the more severe, complex injuries requiring additional rehabilitation compared to those that have minimal deficits. All individuals with a history of SCI would benefit from appropriate community follow tailored to their needs; results of this study highlight the importance of ongoing long-term community follow-up for those who require inpatient rehabilitation post-injury.

Pain has been associated with spasticity in SCI, with a large cross-sectional study ($N = 1579$) demonstrating that individuals with SCI and spasticity had a 2.38 increased odds of reporting a chronic pain problem compared individuals with SCI who did not experience spasticity.[25] The interaction between pain and spasticity is complex, as spasticity can cause pain, and pain can trigger spasticity in a bidirectional relationship. Findings from this study highlight the importance of including questions regarding pain when asking a patient regarding their spasticity history.

Results from this study suggest that the PSFS could be a valuable tool for assessment of spasticity in SCI. Not only is the presence of muscle spasms on the PSFS a predictor of problematic spasticity, it has low burden of use as it can be quickly administered at the time of community discharge. Spasticity is difficult to assess solely with objective clinical measures; the additional use of self-report measures is thought to more accurately capture the experience of spasticity in people with SCI.[26,27]

Anti-spasticity medication prescription at discharge being a predictor for spasticity limiting function in the community may just mean that the affected individuals had more spasticity and thus needed more medications. However, this finding could be concerning, as clinicians hope that appropriately managed spasticity during hospitalization using interventions such as medications will decrease the risk of spasticity impairing function in the long term. This finding highlights the need for ongoing follow-up of these individuals in the long term as well as the need for further research on how to best treat spasticity in the SCI population.

Predictive modeling of development of problematic spasticity

In validation analysis of prediction models, area under the ROC curve values ≥ 0.8 are considered excellent and values ≥ 0.7 are acceptable.[28] The predictive models created in this study provide excellent discrimination with lower boundaries of the CI crossing into acceptable discrimination. In order to utilize the nomograms developed, at the time of community discharge the clinician will need to: (1) review the chart for GCS at the scene of the accident, age at time of injury, admission to rehabilitation, and prescription of anti-spasticity medication at time of discharge; (2) Administer the NRS pain interference for activities, sleep and quality of life as well as the PSFS questionnaires; (3) Perform a detailed neurological examination to ascertain discharge neurological and motor level (which is considered part of standard clinical care at our local acute care and rehabilitation centers), and determine the change in AIS motor score between admission and discharge. An important role of the clinician is to be a steward of resources in settings that often have limited funding. Therefore, it is important to be able to determine those who are higher risk for developing significant secondary medical complications such as problematic spasticity so as to allocate resources (such as referral to a spasticity clinic and regular long-term follow-up with an SCI medicine trained clinician) to those who are most likely to benefit.

Study limitations

Strengths of our study include the prospectively collected data in a large population, the availability of detailed information about patients' initial neurological impairments assessed by trained clinicians, and a validation population of the derived predictive models. Spasticity was assessed using self-report questionnaires; clinical data such as the Modified Ashworth Scale were not collected. There is a reasonable correlation between the physical findings of spasticity on clinical exam and patient-reported spasm severity scores according to the PSFS.[29] Also, it has been hypothesized that a 1-time clinical exam is a weak reflection of general spasticity, and self-report measures may better capture the overall burden of spasticity. Therefore, using self-report questionnaires to determine the presence of spasticity is considered a strength of this study. Potential limitations include that the primary outcome measure was self-reported; results from this study are limited to the SCI population that received their post SCI acute treatment and rehabilitation at the RHSCIR centers involved in the study. We acknowledge that one of the limitations of this study is that we utilized the PSFS and medication usage at discharge, but that the length of stay varied greatly in our patient cohort. Differences in practice and the time between admission to community discharge between centers may affect outcomes.

Therefore, an external validation study is needed to assess the generalizability of these prediction models.[30]

Conclusion

Improving ability to provide an early prognosis on the development of problematic spasticity in the long term allows clinicians to better allocate limited resources, ensure appropriate follow-up and educate patients regarding expected outcomes. Results of the study suggest that there is an opportunity to enhance early rehabilitation efforts especially in those who fit the predictive model for problematic spasticity. These efforts include preventative strategies such as patient education on avoidance of spasticity triggers, and physical therapies such as a stretching program, the standing frame, and electrical therapy for life long management of spasticity. Validated prediction models also assist research (e.g. risk stratification in interventional trials). Further research is needed to confirm the predictive ability of these nomograms in other SCI populations. If demonstrated to be robust, these predictive models can greatly assist clinical care and research in spasticity management following SCI.

Abbreviations

SCI	spinal cord injury
RHSCIR	Rick Hansen Spinal Cord Injury Registry
AIS	American Spinal Injury Association Impairment Scale
PSFS	Penn Spasm Frequency Scale
SCI-HQ	Spinal Cord Injury Health Questionnaire
GCS	Glasgow Coma Scale
NRS	Numeric Rating Scale
ROC	receiver operating characteristic
CI	confidence interval

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Disclaimer statements

Contributors None

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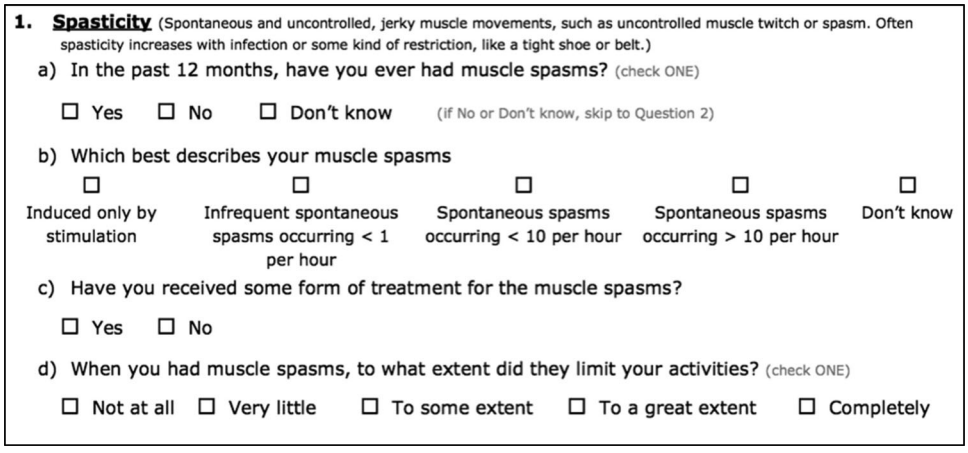
Appendix A. Spinal Cord Injury Health Questionnaire

The Spinal Cord Injury Health Questionnaire (SCI-HQ) is a self-reported questionnaire that assesses the presence of health conditions in community follow-up at 1, 2 and 5 years' post-injury. Below are the questions asked:


1. **Spasticity** (Spontaneous and uncontrolled, jerky muscle movements, such as uncontrolled muscle twitch or spasm. Often spasticity increases with infection or some kind of restriction, like a tight shoe or belt.)

a) In the past 12 months, have you ever had muscle spasms? (check ONE)

☐ Yes ☐ No ☐ Don't know (if No or Don't know, skip to Question 2)

b) Which best describes your muscle spasms

☐	☐	☐	☐	☐
Induced only by stimulation	Infrequent spontaneous spasms occurring < 1 per hour	Spontaneous spasms occurring < 10 per hour	Spontaneous spasms occurring > 10 per hour	Don't know

c) Have you received some form of treatment for the muscle spasms?

☐ Yes ☐ No

d) When you had muscle spasms, to what extent did they limit your activities? (check ONE)

☐ Not at all ☐ Very little ☐ To some extent ☐ To a great extent ☐ Completely

In the expanded RHSCIR dataset the following is encoded: presence of spasticity (yes/no), ongoing treatment for spasticity (yes/no) and functional limitation of activities (yes/no). Treatment for spasticity includes physical therapy, anti-spasticity medication and/or surgery.

Penn Spasm Frequency Scale

The Penn Spasm Frequency Scale (PSFS) is a self-reported questionnaire used to assess spasticity-related muscle spasms. It is composed of 2 Parts. Part 1 is the portion of the self-report measure with items on 5-point scale assessing spasm frequency over the last 7 days.

Part 1: Spasm Frequency

0 = No spasm
1 = Mild spasms induced by stimulation
2 = Infrequent full spasms occurring less than once per hour
3 = Spasms occurring more than once per hour
4 = Spasms occurring more than ten times per hour

Appendix B

Table A1 Detailed data for spasticity requiring treatment in community follow-up.

Category	Characteristic	Level	OR (95% CI)	Variable Importance Probability
Admission				
Demographics	Gender	Female	1	–
		Male	1.06 (0.96, 1.18)	0.436
	Age (10 years)		0.96 (0.93, 0.98)	0.371
	Living arrangement	Alone	1	–
		Not alone	0.94 (0.85, 1.05)	0.363
	Household income	>= 20K	1	–
		< 20K	0.98 (0.85, 1.14)	0.345
	Education	No Diploma or G.E.D	1	–
		Diploma	0.90 (0.80, 1.01)	0.375
Trauma	GCS facility	Mild	1	–
		Moderate	1.12 (0.78, 1.61)	0.425
		Severe	1.04 (0.87, 1.25)	0.443
	GCS field	Mild	1	–
		Moderate	1.38 (1.05, 1.81)	0.798
		Severe	1.06 (0.88, 1.28)	0.68
Medical History	Comorbidities	None	1	–
		At least one	0.98 (0.88, 1.10)	0.359
		Missing	1.03 (0.79, 1.34)	0.131
	Cannabis use at admission	No	1	–
		Yes	1.00 (0.88, 1.15)	0.357
Discharge				
Neurology	AIS	A	1	–
		B	0.93 (0.80, 1.08)	0.372
		C	1.29 (1.06, 1.56)	0.626
		D	1.01 (0.77, 1.32)	0.187
		E	0.93 (0.59, 1.48)	0.367
	AIS motor score (20 points)		0.94 (0.73, 1.22)	0.096
	Increase in AIS motor score (20 points)		1.04 (0.98, 1.10)	0.744
	AIS UEMS (20 points)		1.08 (0.83, 1.40)	0.184
	AIS LEMS (20 points)		1.12 (0.81, 1.53)	0.257
	Neurological level	C1–C8	1	–
		T1–T12	1.07 (0.83, 1.38)	0.4
		L1–S5	0.94 (0.88, 1.61)	0.867
		C1–T12 + L1–S5	0.66 (0.44, 0.98)	0.374
	Motor neuro level	C1–C8	1	–
		T1–T12	0.93 (0.74, 1.17)	0.252
		L1–S5	0.74 (0.54, 1.02)	0.824
		C1–T12 + L1–S5	0.44 (0.31, 0.63)	0.196
Course of care	Operation	No	1	–
		Yes	1.03 (0.89, 1.20)	0.417
	Gabapentin, within 1 month	No	1	–
		Yes	0.94 (0.85, 1.04)	0.385
	Length, inpatient stay (30 days)		0.95 (0.91, 0.99)	0.3
	Rehab	No	1	–
		Yes	1.21 (1.05, 1.40)	0.762
	Length, rehab (30 days)		1.03 (0.98, 1.08)	0.24
Pain	Pain, activity	None	1	–
		Mild	1.02 (0.87, 1.18)	0.45
		Moderate	1.10 (0.93, 1.30)	0.928
		Severe	0.89 (0.71, 1.13)	0.328
	Pain, QOL	None	1	–
		Mild	1.06 (0.91, 1.24)	0.481
		Moderate	1.05 (0.88, 1.25)	0.234
		Severe	1.20 (0.99, 1.47)	0.465
	Pain, sleep	None	1	–
		Mild	0.95 (0.84, 1.08)	0.291
		Moderate	0.91 (0.78, 1.06)	0.458
		Severe	1.16 (0.98, 1.38)	0.296

Continued

Table A1 ***Continued*.**

Category	Characteristic	Level	OR (95% CI)	Variable Importance Probability
Spasticity	PSFS	0	1	–
		1	1.20 (1.07, 1.35)	0.886
		2	1.49 (1.28, 1.75)	0.66
		3	1.37 (1.15, 1.63)	0.682
		4	1.67 (1.28, 2.19)	0.964
	Discharge anti-spasticity medication	No	1	–
		Yes	1.18 (1.04, 1.33)	1

Table A2 Detailed data for spasticity limiting function in community follow-up.

Category	Characteristic	Level	OR (95% CI)	Variable Importance Probability
Admission				
Demographics	Gender	Female	1	–
		Male	1.06 (0.96, 1.18)	0.558
	Age (10 years)		0.96 (0.93, 0.98)	0.98
	Living arrangement	Alone	1	–
		Not alone	0.94 (0.85, 1.05)	0.549
	Household income	≥ 20K	1	–
		< 20K	0.98 (0.85, 1.14)	0.589
	Education	No Diploma or G.E.D	1	–
		Diploma	0.90 (0.80, 1.01)	0.633
Trauma	GCS facility	Mild	1	–
		Moderate	1.12 (0.78, 1.61)	0.741
		Severe	1.04 (0.87, 1.25)	0.525
	GCS field	Mild	1	–
		Moderate	1.38 (1.05, 1.81)	0.888
		Severe	1.06 (0.88, 1.28)	0.536
Medical history	Comorbidities	None	1	–
		At least one	0.98 (0.88, 1.10)	0.553
		Missing	1.03 (0.79, 1.34)	0.052
	Cannabis use at Admission	No	1	-
		Yes	1.00 (0.88, 1.15)	0.6
Discharge				
Neurology	AIS	A	1	–
		B	0.93 (0.80, 1.08)	0.622
		C	1.29 (1.06, 1.56)	0.977
		D	1.01 (0.77, 1.32)	0.499
		E	0.93 (0.59, 1.48)	0.256
	AIS motor score (20 points)		0.94 (0.73, 1.22)	0.428
	Increase in AIS motor score (20 points)		1.04 (0.98, 1.10)	0.849
	AIS UEMS (20 points)		1.08 (0.83, 1.40)	0.461
	AIS LEMS (20 points)		1.12 (0.81, 1.53)	0.434
	Neurological level	C1–C8	1	–
		T1–T12	1.07 (0.83, 1.38)	0.402
		L1–S5	1.19 (0.88, 1.61)	0.475
		C1–T12 + L1–S5	0.66 (0.44, 0.98)	0.756
	Motor neuro level	C1–C8	1	–
		T1–T12	0.93 (0.74, 1.17)	0.369
		L1–S5	0.74 (0.54, 1.02)	0.887
		C1–T12 + L1–S5	0.44 (0.31, 0.63)	0.516
Course of care	Operation	No	1	–
		Yes	1.03 (0.89, 1.20)	0.698
	Gabapentin, within 1 month	No	1	–
		Yes	0.94 (0.85, 1.04)	0.55
	Length, inpatient stay (30 days)		0.95 (0.91, 0.99)	0.727
	Rehab	No	1	–
		Yes	1.21 (1.05, 1.40)	0.818
	Length, rehab (30 days)		1.03 (0.98, 1.08)	0.191

Continued

Table A2 ***Continued*.**

Category	Characteristic	Level	OR (95% CI)	Variable Importance Probability
Pain	Pain, activity	None	1	–
		Mild	1.02 (0.87, 1.18)	0.367
		Moderate	1.10 (0.93, 1.30)	0.937
		Severe	0.89 (0.71, 1.13)	0.525
	Pain, QOL	None	1	–
		Mild	1.06 (0.91, 1.24)	0.465
		Moderate	1.05 (0.88, 1.25)	0.445
		Severe	1.20 (0.99, 1.47)	0.852
	Pain, sleep	None	1	–
		Mild	0.95 (0.84, 1.08)	0.467
		Moderate	0.91 (0.78, 1.06)	0.703
		Severe	1.16 (0.98, 1.38)	0.883
Spasticity	PSFS	0	1	–
		1	1.20 (1.07, 1.35)	0.825
		2	1.49 (1.28, 1.75)	0.998
		3	1.37 (1.15, 1.63)	0.944
		4	1.67 (1.28, 2.19)	0.977
	Discharge anti-spasticity medication	No	1	–
		Yes	1.18 (1.04, 1.33)	0.998